

Claims:

1. A method of decreasing or preventing occlusion of a body vessel by smooth muscle cells, comprising administering an agent that promotes elastin signaling in an amount effective to decrease or prevent occlusion of a body vessel by smooth muscle cells.
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2. A method of decreasing vascular obstruction, comprising administering an agent effective to decrease vascular obstruction, wherein said agent promotes elastin signaling thereby modulating vascular smooth muscle cells sufficiently to decrease vascular obstruction.
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3. A method of promoting actin stress fiber formation in a smooth muscle cell, comprising contacting said smooth muscle cell with an agent that promotes elastin signaling in an amount effective to promote actin stress fiber formation.
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4. A method of promoting actin polymerization in a smooth muscle cell, comprising contacting said smooth muscle cell with an agent that promotes elastin signaling in an amount effective to promote actin polymerization.
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5. A method of increasing the ratio of F:G actin in a smooth muscle cell, comprising contacting said smooth muscle cell with an agent that promotes elastin signaling in an amount effective to increase the ratio of F:G actin.
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6. A method for the treatment or prophylaxis of an obstructive vascular disease, comprising administering an agent that promotes elastin signaling in an amount effective to treat or prophylactically treat said obstructive vascular disease.
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7. A method for preventing stenosis, comprising administering an amount of an agent effective to prevent stenosis, wherein said agent promotes elastin signaling.
- 5 8. A method for the treatment or prophylaxis of restenosis, comprising administering an amount of an agent effective to treat or prophylactically treat restenosis, wherein said agent promotes elastin signaling.
9. The method of claim 1, wherein said body vessel is selected from any of 10 artery, vein, common bile duct, pancreatic duct, kidney duct, esophagus, trachea, urethra, bladder, uterus, ovarian duct, Fallopian tube, vas deferens, prostatic duct, or lymphatic duct.
10. The method of any of claims 3-5, wherein said smooth muscle cell is a 15 vascular smooth muscle cell.
11. The method of claim 1 or 2, further comprising administering a compound that inhibits proliferation of smooth muscle cells.
- 20 12. The method of claim 11, wherein said compound is selected from paclitaxel, rapamycin, actinomycin D, or radioactivity.
13. The method of claim 8, wherein said restenosis occurs following angioplasty.
- 25 14. The method of claim 1 or 2, wherein said agent is administered on a biocompatible device.
15. The method of claim 14, wherein said biocompatible device is an 30 intraluminal device, and wherein said agent is administered to the site of occlusion or vascular obstruction.

16. The method of claim 15, wherein said intraluminal device is selected from a stent, a wire, a catheter, or a sheath.
17. The method of claim 1 or 2, wherein said agent is selected from a nucleic acid, peptide, polypeptide, peptidomimetic, small organic molecule, antisense oligonucleotide, RNAi construct, ribozyme, or antibody.
18. The method of claim 17, wherein said agent promotes elastin signaling by
 - (i) binding to and activating the elastin receptor,
 - (ii) increasing the expression and/or activity of tropoelastin,
 - (iii) increasing the expression and/or activity of a protein that activates the elastin receptor,
 - (iv) activating Gi, or
 - (v) activating RhoA.
19. The method of claim 17, wherein said agent promotes elastin signaling by inhibiting the expression and/or activity of a protein that represses elastin signaling.
20. The method of claim 19, wherein said protein that represses elastin signaling is a protein that promotes the off state of RhoA.
21. The method of claim 20, wherein said protein that promotes the off state of RhoA is a GAP or GDI.
22. The method of claim 17, wherein said agent is selected from tropoelastin, a bioactive fragment of tropoelastin, elastin receptor, a constitutively active elastin receptor, Gi, a constitutively active Gi, RhoA, a constitutively active RhoA, or a GAP.

22. The method of claim 17, wherein said agent is selected from a bioactive fragment of tropoelastin, elastin receptor, a constitutively active elastin receptor, Gi, a constitutively active Gi, RhoA, a constitutively active RhoA, or a GAP.

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23. The method of claim 17, wherein said agent is selected from elastin receptor, a constitutively active elastin receptor, Gi, a constitutively active Gi, RhoA, a constitutively active RhoA, or a GAP.

10 24. The method of claim 17, wherein said agent comprises a polypeptide comprising an amino acid sequence at least 80% identical to any of SEQ ID NO: 2, SEQ ID NO: 3, or SEQ ID NO: 6.

15 25. Use of an agent that promotes elastin signaling in smooth muscle cells in the manufacture of a medicament for the treatment or prevention of occlusion of a vessel.

26. The use of claim 25, wherein said smooth muscle cell is a vascular smooth muscle cell.

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27. The use of claim 25, wherein said vessel is selected from any of artery, vein, common bile duct, pancreatic duct, kidney duct, esophagus, trachea, urethra, bladder, uterus, ovarian duct, Fallopian tube, vas deferens, prostatic duct, or lymphatic duct.

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28. The use of claim 25, wherein said agent is selected from any of a nucleic acid, a peptide, a polypeptide, a peptidomimetic, a small organic molecule, an antibody, an antisense oligonucleotide, an RNAi construct, or a ribozyme.

30 29. The method of claim 1 or 2, wherein said agent is formulated in a pharmaceutically acceptable carrier.

30. A method of screening to identify and/or characterize an elastin activator that promotes elastin signaling in smooth muscle cells, comprising
 - (a) contacting a cell with one or more agents;
 - 5 (b) comparing elastin signaling in said cell in the presence of said one or more agents in comparison to the absence of said one or more agents, wherein an agent that promotes elastin signaling in a cell is an elastin activator.
- 10 31. The method of claim 30, further comprising formulating said agent that promotes elastin signaling in a pharmaceutically acceptable carrier.
32. An agent identified by the method of claim 30, wherein said agent has any of the following functions:
 - 15 (i) increases actin stress fiber formation in smooth muscle cells,
 - (ii) increases expression of vinculin in smooth muscle cells,
 - (iii) increases focal adhesion formation in smooth muscle cells,
 - (iv) inhibits dedifferentiation of smooth muscle cells,
 - (v) promotes actin polymerization in smooth muscle cells,
 - 20 (vi) increases the ratio of F:G actin in smooth muscle cells,
 - (vii) decreases or inhibits occlusion of a vessel,
 - (viii) decreases or inhibits vascular obstruction,
 - (ix) decreases or inhibits restenosis, or
 - (x) prevents stenosis.
- 25 33. The agent of claim 32 formulated in a pharmaceutically acceptable carrier.
34. The method of claim 30, wherein screening of one or more agents comprises screening a library of agents.

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35. The method of claim 34, wherein said one or more agents is a nucleic acid, peptide, polypeptide, small organic molecule, antibody, antisense oligonucleotide, ribozyme, or RNAi construct.

5 36. A method of conducting a drug discovery business comprising:

- (a) identifying, by the assay of claim 30, one or more agents which promote elastin signaling;
- (b) conducting therapeutic profiling of an agent identified for efficacy and toxicity in one or more animal models; and
- 10 (c) formulating a pharmaceutical preparation including one or more agents identified as having an acceptable therapeutic profile.

37. The method of claim 36, further including establishing a system for distributing the pharmaceutical preparation for sale.

15 38. The method of claim 36 or 37, further including establishing a sales group for marketing the pharmaceutical preparation.

39. A method of screening to identify and/or characterize an elastin receptor, comprising

20 (a) expressing at least one candidate receptor in a cell which is not responsive to elastin signaling;

- (b) expressing GiRK 1 and GiRK 4 in said same cell, whereby said cell expresses

25 (c) a heteromultimeric GiRK channel;

- (d) contacting said cell with tropoelastin or a bioactive fragment thereof;

30 (e) measuring activity of said heteromultimeric GiRK channel in the presence of tropoelastin or a bioactive fragment thereof in comparison to the activity of said heteromultimeric GiRK channel in the absence of tropoelastin or a bioactive fragment thereof;

wherein activation of said heteromultimeric GiRK channel in the presence of tropoelastin or a bioactive fragment thereof indicates that the candidate receptor is an elastin receptor.

5 40. The method of claim 39, wherein said cell is an oocyte.

41. The method of claim 40, wherein said oocyte is a *Xenopus* oocyte.

42. The method of claim 39, wherein said at least one candidate receptor is a
10 library of candidate receptors.

43. The method of claim 42, wherein said library of candidate receptors is a
library of G-protein coupled receptors.

15 44. The method of claim 39, wherein activation of said heteromultimeric GiRK
channel is measured using whole cell clamping

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